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POTENTIAL ENERGY CALCULATIONS OF TREPTILAMINUM: AN ANTICHOLINERGIC DRUGS

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Semiempirical conformational energy calculations were performed for the treptilaminum and only non bonded interactions are considered. The calculations suggest that treptilaminum adopts limited allowed conformations. It is likely that a mixture of conformational states for the interaction with the receptor.

Key words: Potential energy, Treptilaminum, Energy calculation.

INTRODUCTION

Treptilaminum, 2,- (tricyclo-(2.2.1.0.) Y Lidene) benzyloxy triethylamine, acts as atropine like antagonist of acetylcholine at the parasympathetic post-ganglionic muscarinic receptor. Its pharmacological action is approximately equal to that of atropine and *N*-bromobutyl hyoscine[1].It is antispasmodic in nature and devoid of side effects of similar types of anticholinergic agents.

Treptilaminum, crystallizes in the space group $P2_1$ with dimensions a = 11.267, b = 31.61, c = 10.803 A, $\beta = 98.71^{\circ}$.

The present work describes the conformation of treptilaminum (molecule A) and calculatilons of potential energy based on the Kitaigorodsky function [2]. Sord computer Mark M-68 was used throughout this work.

METHOD OF CALCULATION

The mathematical details have already been published by us [3,4] and Kitaigorodsky [2] Fig. 3 shows the structure of treptilaminum and three parts of the structure are labelled as I, II, III. The rotation of ring I about C_1-C_2 the rotation of II about the bond C_1-0_2 and the rotation of ring III about the bond C_1-C_1 can be designated as W_1, W_2 and W_3 respectively.

The positions of atoms in rings I, II, III can be calculated by rotating ring I about C_1-C_2, ring II about C_1-0_1, and ring III about C_1-C_8. As a first step the conformation of ring I and ring II are determined. The pairs of atoms selected are C_7-C_{15}, C_3-C_{15}, C_6-C_{15}, C_7-C_{16}, C_7-C_{17}, C_7-C_{18}. Similarly the pairs of atoms selected for ring II and ring III are C_{15}-C_8, C_{15}-C_9, C_{15}-C_{12}, C_{15}-C_{13}, C_{17}-C_9, C_{17}-C_{13}, C_{17}-C_{12}, C_{17}-C_8, C_{18}-C_9, C_{18}-C_{10}, C_{18}-C_{12}, O-C_9, O-O_{13}, O-C_{12}.

RESULTS AND DISCUSSION

Conformational maps for the parts. I, II and II, III are given in (Fig. 1) and (Fig. 2) respectively. The contour map

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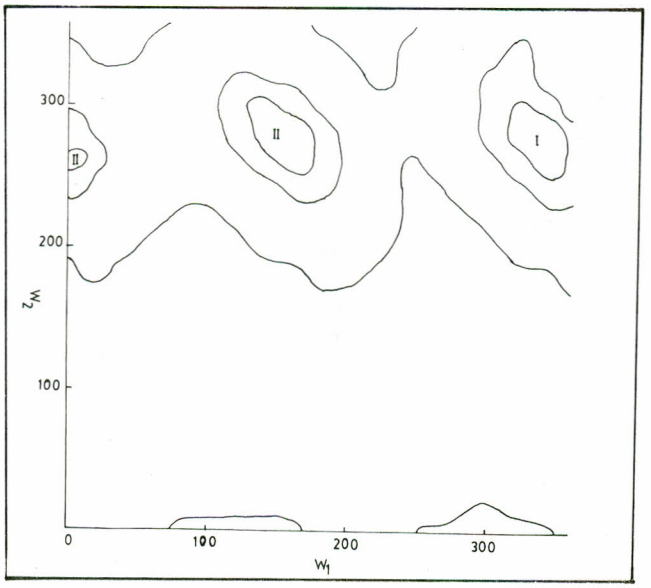

Fig. 1. Energy contours for treptilaminum for the rings I,II.

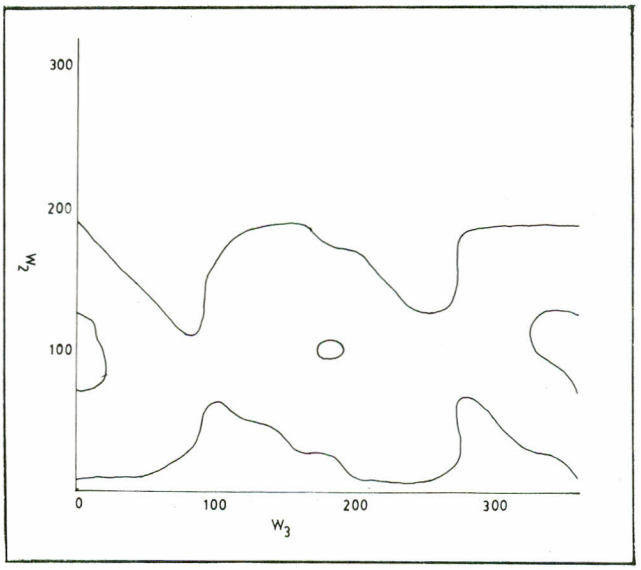

Fig. 2. Energy contours for treptilaminum for the rings II, III.

(Fig.1) indicates that there is serious type of over- lapping (ring I, ring II) at W_1=320°, W_2=280°, W_1=160°, W_2=280°, W_1=O°, W_2=260°. These regions are marked as I, II, III

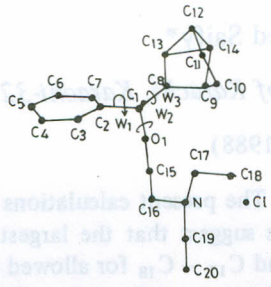

Fig.3. Structure of treptilaminum.

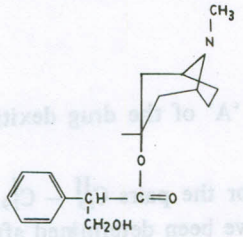

Fig.4. Structure of atropine.

(Fig. 1.) and IV, V, VI (Fig. 2.) The overall picture is that the molecule adopts a limited allowed conformations. Calculations of conformational analysis for treptilaminum in space produce results which are in good agreement with experimental data derived from crystallographic studies. If series of molecules having similar type of activity atropine [Fig.4), buscopan (Fig.5), gastropine (Fig.6) with varying activities are studied from conformational point of view, it may be possible to define precise conformation which is essential for activity. For this type of work more detailed

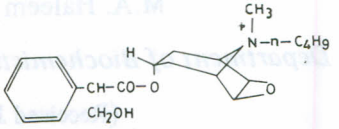

Fig.5. Structure of buscopan.

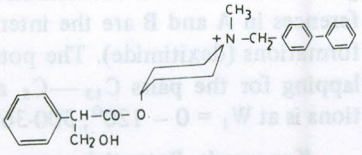

Fig. 6. Structure of gastropine.

calculations will be required. Such studies can give informations about detailed picture of active receptor site and conformation of drugs for the interaction with the receptor than those currently found in the literature.

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